Remarks

Amendments to the Claims

Claim 1 is amended the recite that the polynucleotide is within the host cell genome, within a plasmid, or within a replicon. Support is at the paragraph spanning pages 4 and 5.

New claims 45-48 recite that the polynucleotide is within the host cell genome, within a plasmid, within a DNA replicon, and within an RNA replicon, respectively. Support is at the paragraph spanning pages 4 and 5.

Rejection of Claims 1-13, 25, 27, 36, and 38 Under 35 U.S.C. § 112 ¶ 1

Claims 1-13, 25, 27, 36, and 38 stand rejected under 35 U.S.C. 112 ¶ 1 as not enabled. The Patent Office contends it would require undue experimentation to use linear DNA, RNA or "any virus including retrovirus (especially HIV)." Office Action at page 3.

To advance prosecution, Applicants have amended claim 1 to recite that polynucleotide encoding the immunogen is within the host cell genome, within a plasmid, or within a replicon.

The test of enablement is whether the specification provides sufficient guidance that one reasonably skilled in the art could make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). In this case, one of ordinary skill in the art certainly could make and use the full scope of the claimed subject matter by following the teachings of the specification in view of the prior art.

The Examiner acknowledges that the use of plasmids is enabled. Office Action at page 3. Like plasmids, those of ordinary skill in the art would readily be able to make and use bacteria containing polynucleotides within the bacteria genome or polynucleotides within replicons. Plasmids and replicons are highly similar; indeed, in most cases the terms are often synonymous.

Replicons are nucleic acids having a single origin of replication. Plasmids with only one replicating genetic unit are replicons. However, plasmids can contain more than one replicating genetic unit; *i.e.*, more than one replicon. See, for example, Sambrook: [1]

> Usually a plasmid will contain only one origin of replication together with its associated cis-acting control elements (the whole genetic unit being defined as a 'replicon'). Very rarely, however, plasmids that been generated by fusion will contain more than one replicon; in such cases, only one replicon is active.

Because replicons propagate in bacteria, they can be maintained within bacteria as readily as plasmids. One of ordinary skill in the art could therefore readily make and use bacterial host cells containing plasmids or replicons. Further, because bacteria harboring polynucleotides in their genomic DNA are old in the art, one of ordinary skill in the art could readily make and use a host cell with a polynucleotide within the host cell genome. See for example, U.S. Pat. No. 5,695,976.[2]

Finally, Applicants traverse the portion of the rejection asserting that linear nucleic acids are not enabled. While circular plasmids and replicons are more common, bacterial plasmids and replicons can be linear, as discussed in Girons[3] page 1809, col.1 ¶3 to page 1810 col. 1 ¶1.

One of ordinary skill in the art would readily be able to make and use bacterial host cells containing polynucleotides regardless of whether the polynucleotide was within the host genome, within a plasmid, or within a DNA or RNA replicon. Amended claim 1, dependent claims 2-13, 25, 27, 36, and 38, and new claims 45-48 are enabled.

Please withdraw the rejection.

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[1] Sambrook *et al.*, Molecular Cloning: a Laboratory Manual 2nd Edn, 1989. Vol 1, Page 1.3. A copy is enclosed with the accompanying information disclosure statement.

[2] Made of record in accompanying information disclosure statement.

[3] Girons *et al.*, "Molecular biology of the Borrelia, bacteria with linear replicons," Microbiology. 1994 Aug;140 (Pt 8):1803-16. A copy is enclosed with the accompanying information disclosure statement.

Rejection of Claims 1, 2, 5-8, 9, 12, 13, 25, 27, 36, and 38 Under 35 U.S.C. § 103(a)

Claims 1, 2, 5-8, 9, 12, 13, 25, 27, 36, and 38 stand rejected as obvious over Xu,[4] supported by zur Megede,[5] in view of Masschalck,[6] and Raettig.[7] Applicant respectfully traverses the rejection.

A declaration under 37 C.F.R § 1.131 of the sole inventor, Dr. Feng Xu, was provided in the response filed November 25, 2009 to establish the Xu reference is not prior art to the present application. The Patent Office contends the declaration is defective for three reasons. First, the Patent Office asserts the declaration is defective because the "declaration does not provide notebook dates for the data." Office Action at page 5. A declaration under 37 C.F.R. § 1.131 need not provide dates. The applicant may "merely allege that the acts referred to occurred prior to a specified date." M.P.E.P. § 715.07 II (8th ed. 2007). Dr. Xu states clearly that all work described in the declaration was performed before October 25, 2002. Xu Declaration ¶ 2.

Second, the Patent Office contends the declaration is defective because the "declaration does not address the fact that there were co-authors on the Xu reference that appear to have contributed to the claimed invention." Office Action at page 5. A declaration under 37 C.F.R. § 1.131 to antedate a cited reference does not require the declarant to address other co-authors of a

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[4] Xu *et al.*, "Immunogenicity of an HIV-1 gag DNA vaccine carried by attenuated Shigella," Vaccine. 2003 Jan 30;21(7-8):644-8.

[5] zur Megede *et al.*, "Increased expression and immunogenicity of sequence-modified human immunodeficiency virus type 1 gag gene," J Virol. 2000 Mar;74(6):2628-3.

[6] Masschalck *et al.*, "Inactivation of gram-negative bacteria by lysozyme, denatured lysozyme, and lysozyme-derived peptides under high hydrostatic pressure," Appl Environ Microbiol. 2001 Jan;67(1):339-44.

[7] Raettig, "An oral enteritis-vaccine composed of twelve heat-inactivated Enterobacteriaceae 3. Communication: studies on efficacy tests in mice protection tests," Zentralbl Bakteriol Mikrobiol Hyg A. 1981 Nov;250(4):511-20, abstract.

paper. An explanation of the roles of the Xu co-authors would be relevant only had the Applicant chosen to remove the Xu reference with a declaration under 37 C.F.R. § 1.132. See M.P.E.P. § 715.01(c)(I) (8th ed., Rev. 2007):

> Where the applicant is one of the co-authors of a publication cited against his or her application, he or she may overcome the rejection by filing an affidavit or declaration under 37 CFR 1.131. Alternatively, the Applicant may overcome the rejection by filing a specific affidavit or declaration under 37 CFR 1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone indicating that applicant is the sole inventor and that the others were merely working under his or her direction is sufficient to remove the publication as a reference under 35 U.S.C. 102(a).

Dr. Xu's declaration establishes a date of actual reduction to practice of the claimed invention before the Xu paper became available as a reference under 35 U.S.C. § 102(a). The identity of the authors on the Xu paper and their contribution to the Xu paper's teachings is irrelevant.

Finally, the Patent Office contends the declaration is defective because the "declaration does not state that Xu alone demonstrated the claimed invention prior to 10-25-02." Office Action at page 5. As indicated in M.P.E.P. § 715.01(c)(I), quoted above, Rule 132—not Rule 131—requires a declarant to state that s/he is the sole inventor. In any event, in the signed inventor's declaration filed September 27, 2006, Dr. Xu declares he believes he is the original, first, and sole inventor of the claimed subject matter.

The Xu declaration is a proper declaration under 37 C.F.R. § 1.131 and established that the Xu paper is not prior art to the present application. With the Xu paper removed as a reference, the rejection relies only on the asserted combination of zur Megede, Masschalck, and Raettig, which is insufficient to support a *prima facie* case of obviousness. Zur Megede teaches modified HIV gene sequences in plasmids for improved expression, including the use of CMV promoters in the plasmids. Masschalck teaches lyzozyme inactivation of gram-negative bacteria,

including *Shigella*. The Raettig abstract teaches heat-inactivation of *Shigella*. Even if combined, the disclosures of these references do not teach or suggest all elements of independent claims 1 or 8. Thus, neither independent claims 1 and 8 nor their dependent claims are *prima facie* obvious over the cited references.

Please withdraw the rejection.

Rejection of Claims 1-13, 25, 27, 36, and 38 Under 35 U.S.C. § 103(a)

Claims 1-13, 25, 27, 36, and 38 stand rejected as obvious over Xu supported by zur Megede in view of Masschalck and Raettig and further in view of abstracts of Chang[8] and Kruithof.[9] Applicant respectfully traverses the rejection.

As explained above, Xu is not a prior art reference to the pending claims. Neither Chang nor Kruithof cures the deficiencies of the asserted combination of zur Megede, Masschalck, and Raettig. The Chang abstract teaches killing organisms, including *Shigella*, by UV-treatment. The Kruithof abstract teaches several approaches to killing bacteria, including treatment with ozone, UV, or peroxide, as a means to control bacterial contamination of water. Neither abstract teaches or suggests expressing an immunogen in a mammal by administering a bacterial host cell comprising a polynucleotide encoding the immunogen, wherein the bacterial cell cannot use its own machinery to express the encoded immunogen. Even if combined, the disclosures of zur Megede, Masschalck, Raettig, Chang, and Kruithof do not teach or suggest all elements of independent claims 1 or 8. Thus, neither independent claims 1 and 8 nor their dependent claims are *prima facie* obvious over the cited references.

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[8] Chang *et al.*, "UV inactivation of pathogenic and indicator microorganisms," Appl Environ Microbiol. 1985 Jun;49(6):1361-5, abstract.

[9] Kruithof *et al.*, "UV/H_2O_2-treatment: The ultimate solution for pesticide control and disinfection," Proceedings-Annual Conference, American Water Works assoc. 2000, p331-334, abstract.

Please withdraw the rejection.

Respectfully submitted,

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